#5

FIG. 1

Sequence of human APRIL (SEQ ID NOS: 1 and 2)

Human G70 cDNA (SEQ ID NO 1)
Length: 1465 bp

```
   1  GCCAACCTTC CCTCCCCCAA CCCTGGGGCC GCCCCAGGGT TCCTGCGCAC
  51  TGCCTGTTCC TCCTGGGTGT CACTGGCAGC CCTGTCCTTC CTAGAGGGAC
 101  TGGAACCTAA TTCTCCTGAG GCTGAGGGAG GGTGGAGGGT CTCAAGGCAA
 151  CGCTGGCCCC ACGACGGAGT GCCAGGAGCA CTAACAGTAC CCTTAGCTTG
 201  CTTTCCTCCT CCCTCCTTTT TATTTTCAAG TTCCTTTTTA TTTCTCCTTG
 251  CGTAACAACC TTCTTCCCTT CTGCACCACT GCCCGTACCC TTACCCGCCC
 301  CGCCACCTCC TTGCTACCCC ACTCTTGAAA CCACAGCTGT TGGCAGGGTC
 351  CCCAGCTCAT GCCAGCCTCA TCTCCTTTCT TGCTAGCCCC CAAAGGGCCT
 401  CCAGGCAACA TGGGGGGCCC AGTCAGAGAG CCGGCACTCT CAGTTGCCCT
 451  CTGGTTGAGT TGGGGGGCAG CTCTGGGGGC CGTGGCTTGT GCCATGGCTC
 501  TGCTGACCCA ACAAACAGAG CTGCAGAGCC TCAGGAGAGA GGTGAGCCGG
 551  CTGCAGGGGA CAGGAGGCCC CTCCCAGAAT GGGGAAGGGT ATCCCTGGCA
 601  GAGTCTCCCG GAGCAGAGTT CCGATGCCCT GGAAGCCTGG GAGAGTGGGG
 651  AGAGATCCCG GAAAAGGAGA GCAGTGCTCA CCCAAAAACA GAAGAAGCAG
 701  CACTCTGTCC TGCACCTGGT TCCCATTAAC GCCACCTCCA AGGATGACTC
 751  CGATGTGACA GAGGTGATGT GGCAACCAGC TCTTAGGCGT GGGAGAGGCC
 801  TACAGGCCCA AGGATATGGT GTCCGAATCC AGGATGCTGG AGTTTATCTG
 851  CTGTATAGCC AGGTCCTGTT TCAAGACGTG ACTTTCACCA TGGGTCAGGT
 901  GGTGTCTCGA GAAGGCCAAG GAAGGCAGGA GACTCTATTC CGATGTATAA
 951  GAAGTATGCC CTCCCACCCG GACCGGGCCT ACAACAGCTG CTATAGCGCA
1001  GGTGTCTTCC ATTTACACCA AGGGGATATT CTGAGTGTCA TAATTCCCCG
1051  GGCAAGGGCG AAACTTAACC TCTCTCCACA TGGAACCTTC CTGGGGTTTG
1101  TGAAACTGTG ATTGTGTTAT AAAAAGTGGC TCCCAGCTTG GAAGACCAGG
1151  GTGGGTACAT ACTGGAGACA GCCAAGAGCT GAGTATATAA AGGAGAGGGA
1201  ATGTGCAGGA ACAGAGGCGT CTTCCTGGGT TTGGCTCCCC GTTCCTCACT
1251  TTTCCCTTTT CATTCCCACC CCCTAGACTT TGATTTTACG GATATCTTGC
1301  TTCTGTTCCC CATGGAGCTC CGAATTCTTG CGTGTGTGTA GATGAGGGGC
1351  GGGGGACGGG CGCCAGGCAT TGTTCAGACC TGGTCGGGGC CCACTGGAAG
1401  CATCCAGAAC AGCACCACCA TCTAACGGCC GCTCGAGGGA AGCACCCGGC
1451  GGTTTGGGCG AAGTC
```

The proposed transmembrane domains are boxed

human G70 protein sequence (SEQ ID NO 2)

```
   1  MPASSPFLLA PKGPPGNMGG PVREPALSVA LWLSWGAALG AVACAMALLT
  51  QQTELQSLRR EVSRLQGTGG PSQNGEGYPW QSLPEQSSDA LEAWESGERS
 101  RKRRAVLTQK QKKQHSVLHL VPINATSKDD SDVTEVMWQP ALRRGRGLQA
 151  QGYGVRIQDA GVYLLYSQVL FQDVTFTMGQ VVSREGQGRQ ETLFRCIRSM
 201  PSHPDRAYNS CYSAGVFHLH QGDILSVIIP RARAKLNLSP HGTFLGFV
```

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FIG. 2A

Sequence of mouse G70 (SEQ ID NOS: 3 and 4)

Mouse G70 (SEQ ID NO 3)

```
   1  CATGCCGAGT GCTTTGTGTG TGTTACCTGC TCTAAGAAGC TGGCTGGGCA
  51  GCGTTTCACC GCTGTGGAGG ACCAGTATTA CTGCGTGGAT TGCTACAAGA
 101  ACTTTGTGGC CAAGAAGTGT GCTGGATGCA AGAACCCCAT CACTGGGTTT
 151  GGTAAAGGCT CCAGTGTGGT GGCCTATGAA GGACAATCCT GGCACGACTA
 201  CTGCTTCCAC TGCAAAAAAT GCTCCGTGAA TCTGGCCAAC AAGCGCTTTG
 251  TATTTCATAA TGAGCAGGTG TATTGCCCTG ACTGTGCCAA AAAGCTGTAA
 301  CTTGACGGCT GCCCTGTCCT TCCTAGATAA TGGCACCAAA TTCTCCTGAG
 351  GCTAGGGGGG AAGGAGTGTC AGAGTGTCAC TAGCTCGACC CTGGGGACAA
 401  GGGGGACTAA TAGTACCCTA GCTTGATTTC TTCCTATTCT CAAGTTCCTT
 451  TTTATTTCTC CCTTGCGTAA CCCGCTCTTC CCTTCTGTGC CTTTGCCTGT
 501  ATTCCCACCC TCCCTGCTAC CTCTTGGCCA CCTCACTTCT GAGACCACAG
 551  CTGTTGGCAG GGTCCCTAGC TCATGCCAGC CTCATCTCCA GGCCACATGG
 601  GGGGCTCAGT CAGAGAGCCA GCCCTTTCGG TTGCTCTTTG GTTGAGTTGG
 651  GGGGCAGTTC TGGGGGCTGT GACTTGTGCT GTCGCACTAC TGATCCAACA
 701  GACAGAGCTG CAAAGCCTAA GGCGGGAGGT GAGCCGGCTG CAGCGGAGTG
 751  GAGGGCCTTC CCAGAAGCAG GGAGAGCGCC CATGGCAGAG CCTCTGGGAG
 801  CAGAGTCCTG ATGTCCTGGA AGCCTGGAAG GATGGGGCGA AATCTCGGAG
 851  AAGGAGAGCA GTACTCACCC AGAAGCACAA GAAGAAGCAC TCAGTCCTGC
 901  ATCTTGTTCC AGTTAACATT ACCTCCAAGG ACTCTGACGT GACAGAGGTG
 951  ATGTGGCAAC CAGTACTTAG GCGTGGGAGA GGCCTGGAGG CCCAGGGAGA
1001  CATTGTACGA GTCTGGGACA CTGGAATTTA TCTGCTCTAT AGTCAGGTCC
1051  TGTTTCATGA TGTGACTTTC ACAATGGGTC AGGTGGTATC TCGGGAAGGA
1101  CAAGGGAGAA GAGAAACTCT ATTCCGATGT ATCAGAAGTA TGCCTTCTGA
1151  TCCTGACCGT GCCTACAATA GCTGCTACAG TGCAGGTGTC TTTCATTTAC
1201  ATCAAGGGGA TATTATCACT GTCAAAATTC CACGGGCAAA CGCAAAACTT
1251  AGCCTTTCTC CGCATGGAAC ATTCCTGGGG TTTGTGAAAC TATGATTGTT
1301  ATAAAGGGGG TGGGGATTTC CCATTCCAAA AACTGGCTAG ACAAAGGACA
1351  AGGAACGGTC AAGAACAGCT CTCCATGGCT TTGCCTTGAC TGTTGTTCCT
1401  CCCTTTGCCT TTCCCGCTCC CACTATCTGG GCTTTGACTC CATGGATATT
1451  AAAAAAGTAG AATATTTTGT GTTTATCTCC CAAAAA
```

FIG. 2B

Mouse G70 Length: 241 (SEQ ID NO 4)

```
      1  MPASSPGHMG GSVREPALSV ALWLSWGAVL GAVTCAVALL IQQTELQSLR
     51  REVSRLQRSG GPSQKQGERP WQSLWEQSPD VLEAWKDGAK SRRRRAVLTQ
    101  KHKKKHSVLH LVPVNITSKD SDVTEVMWQP VLRRGRGLEA QGDIVRVWDT
    151  GIYLLYSQVL FHDVTFTMGQ VVSREGQGRR ETLFRCIRSM PSDPDRAYNS
    201  CYSAGVFHLH QGDIITVKIP RANAKLSLSP HGTFLGFVKL *
```

G-70 FLAG des92 (smuG70) Strain #4081 (SEQ ID NO 19):

```
MDYKDDDDKKHKKKHSVLHLVPVNITSKDSDVTEVMWQPVLRRGRGLEAQGDIVRVWDTGIY
LLYSQVLFHDVTFTMGQVVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDII
TVKIPRANAKLSLSPHGTFLGFVKL*
```

FIG. 3

Alignm. of human and mouse G70

```
mouse:   1   MPASS---------PGHMGGSVREPALSVALWLSWGAVLGAVTCAVALLIQQTELQSLRR   51
             MPASS          PG+MGG VREPALSVALWLSWGA LGAV CA+ALL QQTELQSLRR
human:   1   MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRR   60

mouse:   52  EVSRLQRSGGPSQKQGERPWQSLWEQSPDVLEAWKDGAKSRRRRAVLTQKHKKKHSVLHL   111
             EVSRLQ +GGPSQ     PWQSL EQS D LEAW+ G +SR+RRAVLTQK KK+HSVLHL
human:   61  EVSRLQGTGGPSQNGEGYPWQSLPEQSSDALEAWESGERSRKRRAVLTQKQKKQHSVLHL   120

mouse:   112 VPVNITSKD-SDVTEVMWQPVLRRGRGLEAQGDIVRVWDTGIYLLYSQVLFHDVTFTMGQ   170
             VP+N TSKD SDVTEVMWQP LRRGRGL+AQG  VR+ D G+YLLYSQVLF DVTFTMGQ
human:   121 VPINATSKDDSDVTEVMWQPALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQ   180

mouse:   171 VVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDIITVKIPRANAKLSLSP   230
             VVSREGQGR+ETLFRCIRSMPS PDRAYNSCYSAGVFHLHQGDI++V IPRA AKL+LSP
human:   181 VVSREGQGRQETLFRCIRSMPSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNLSP   240

mouse:   231 HGTFLGFVKL 240
             HGTFLGFVKL
human:   241 HGTFLGFVKL 250
```

FIG. 4A

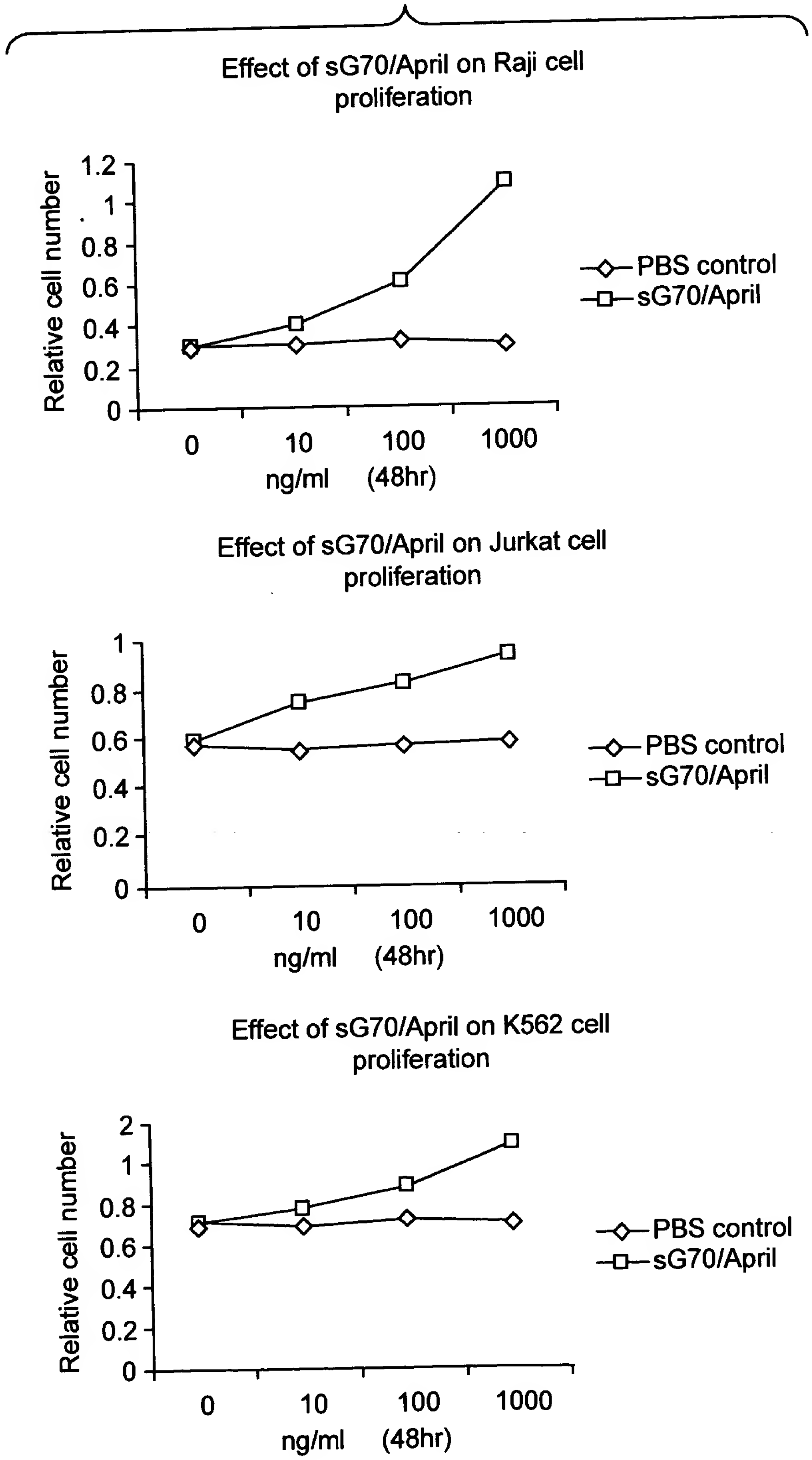

Effect of sG70/April on Raji cell proliferation
Relative cell number
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April
Effect of sG70/April on Jurkat cell proliferation
Relative cell number
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April
Effect of sG70/April on K562 cell proliferation
Relative cell number
2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April

FIG. 4B

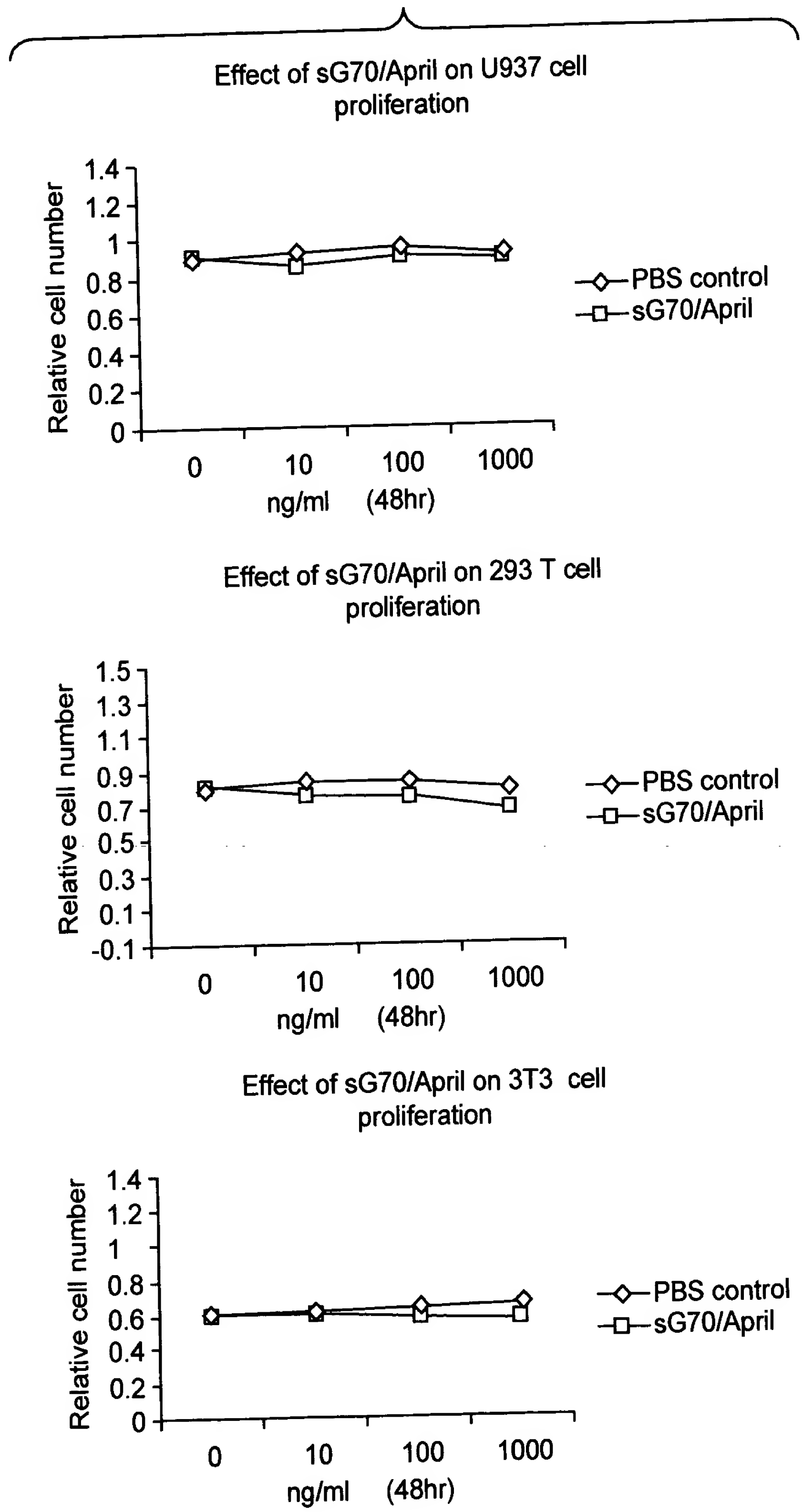

Effect of sG70/April on U937 cell proliferation
Relative cell number
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April
Effect of sG70/April on 293 T cell proliferation
Relative cell number
1.5
1.3
1.1
0.9
0.7
0.5
0.3
0.1
-0.1
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April
Effect of sG70/April on 3T3 cell proliferation
Relative cell number
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April

FIG. 5A

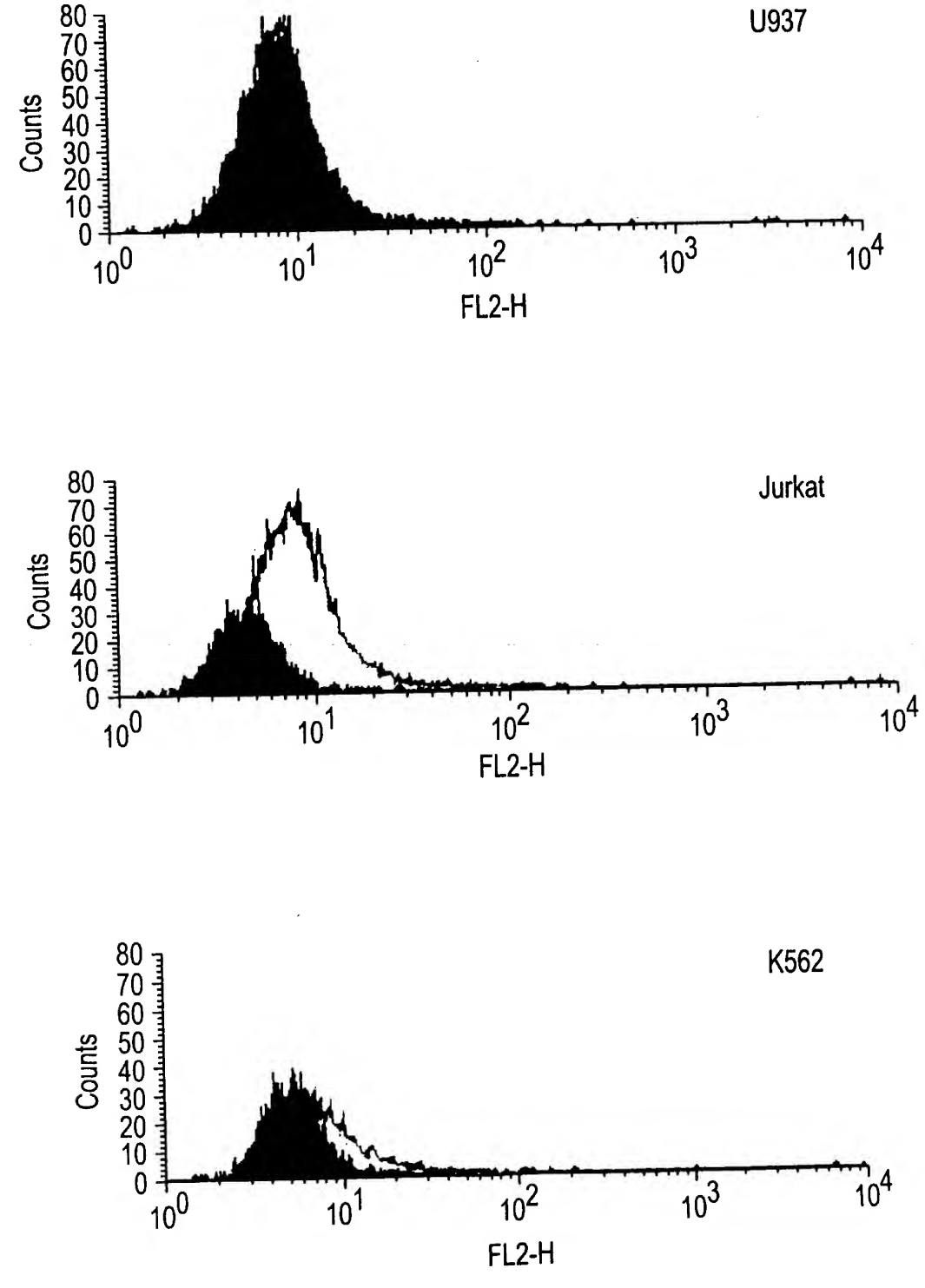

U937
Counts
80
70
60
50
40
30
20
10
0
10^0
10^1
10^2
10^3
10^4
FL2-H
Jurkat
Counts
FL2-H
K562
Counts
FL2-H

FIG. 5B-1

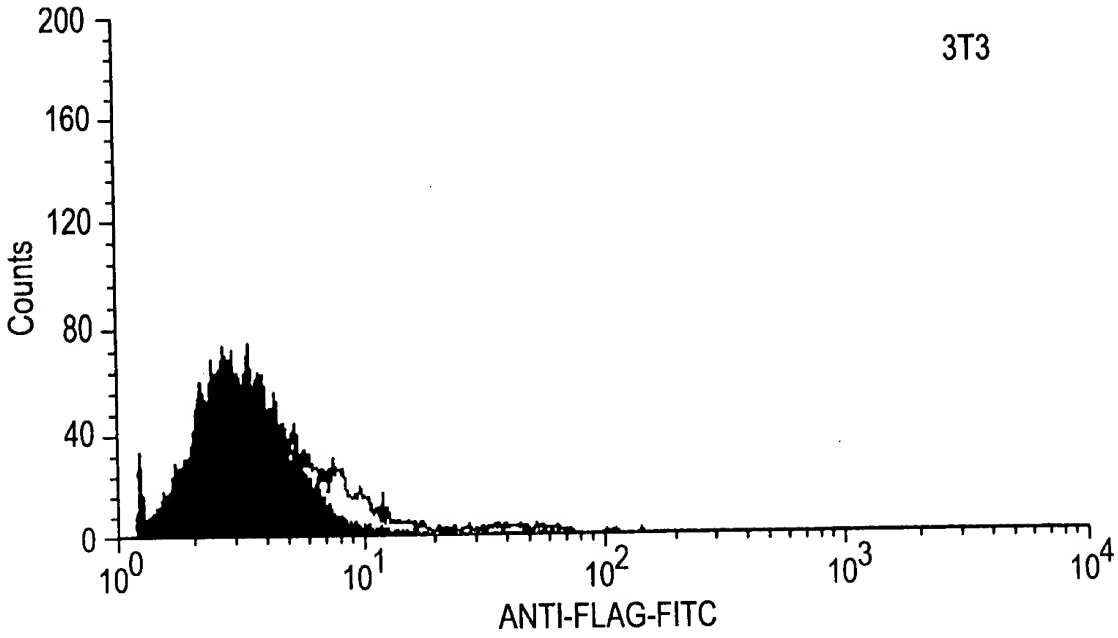


FIG. 5B-2

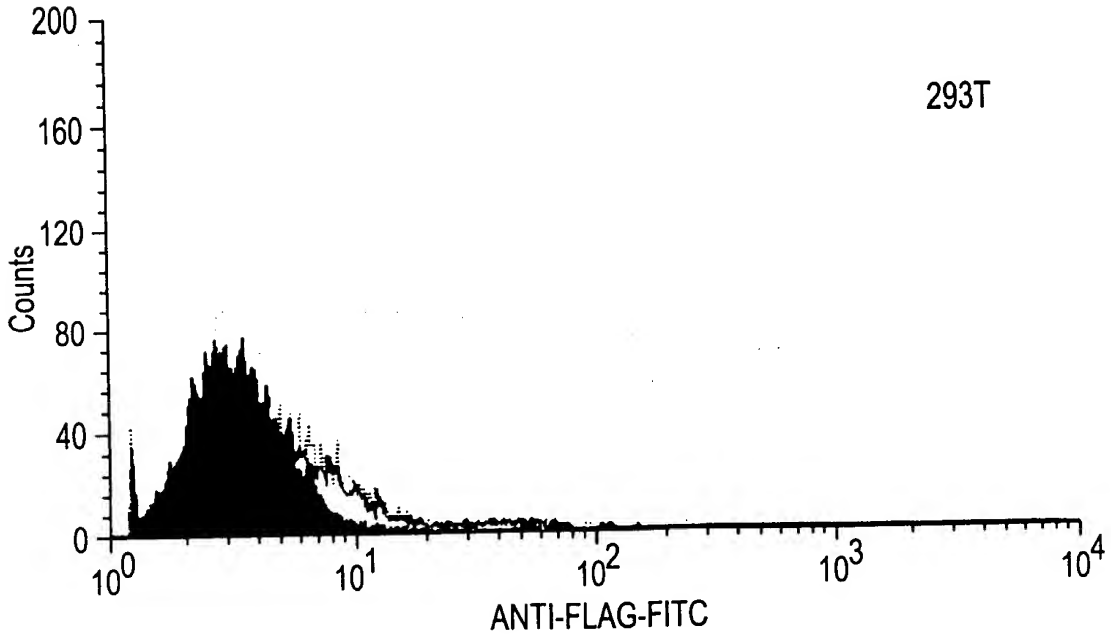


FIG. 5B-3

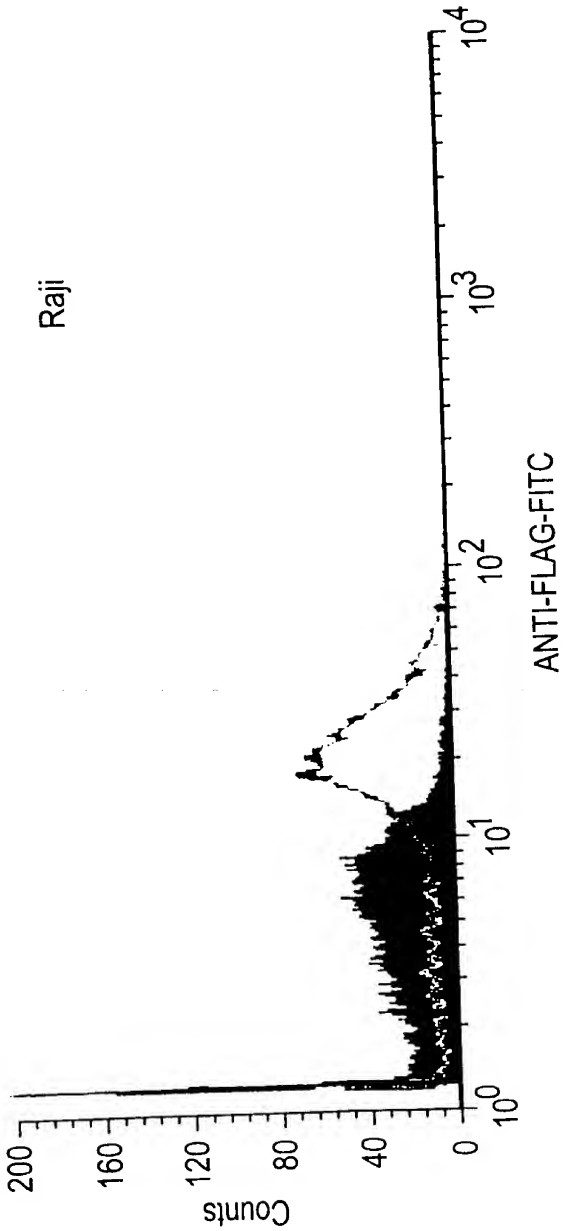
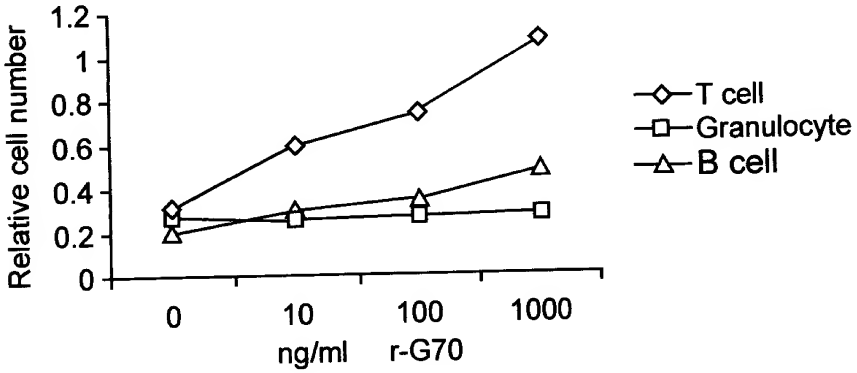

Raji
Counts
200
160
120
80
40
0
10^0
10^1
10^2
10^3
10^4
ANTI-FLAG-FITC

FIG. 6

The effect of r-G70/April on human peripheral blood B cell, T cell and Granucolyte



The effect of IL-2 and G70/April on human peripheral T cell proliferation

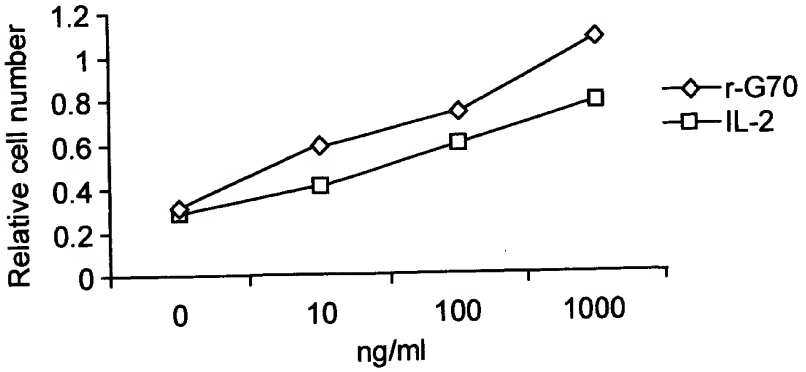


FIG. 7

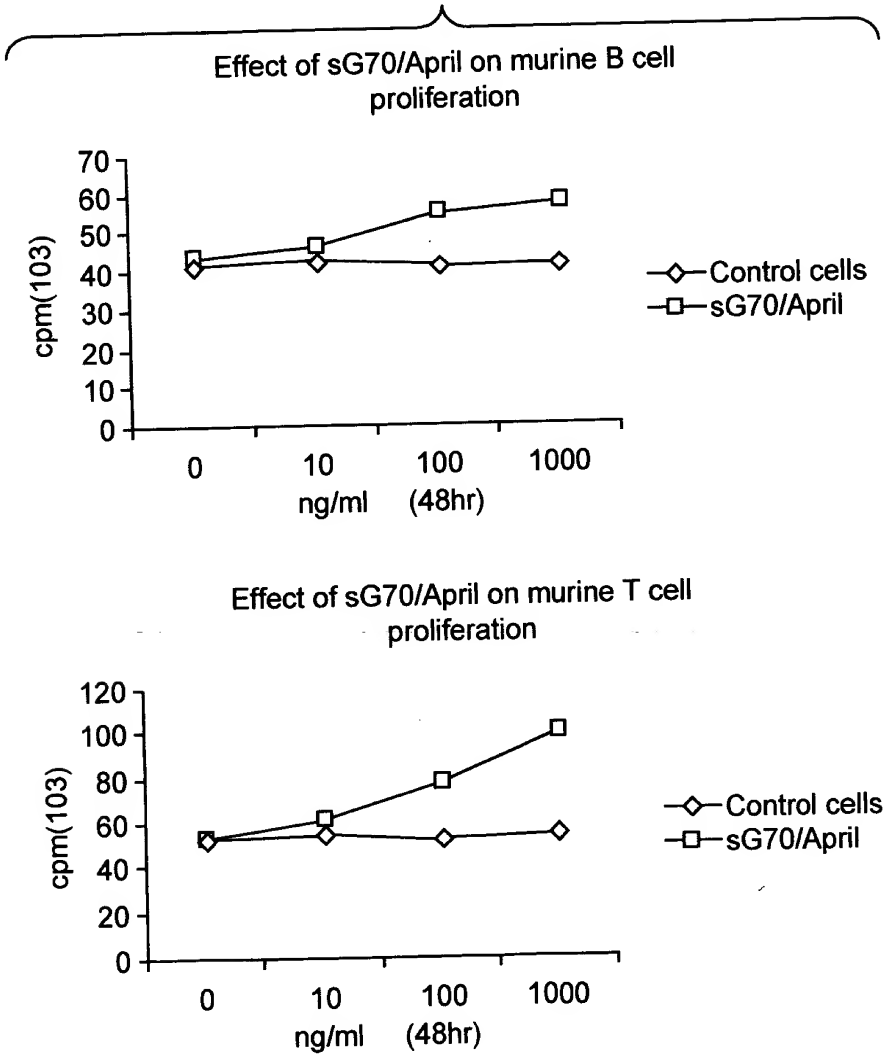

Effect of sG70/April on murine B cell proliferation
cpm(103)
70
60
50
40
30
20
10
0
0
10
100
1000
ng/ml
(48hr)
Control cells
sG70/April
Effect of sG70/April on murine T cell proliferation
cpm(103)
120
100
80
60
40
20
0
0
10
100
1000
ng/ml
(48hr)
Control cells
sG70/April

FIG. 8

Effect of G70/April on murine T cell proliferation costimulated through CD28 antibody

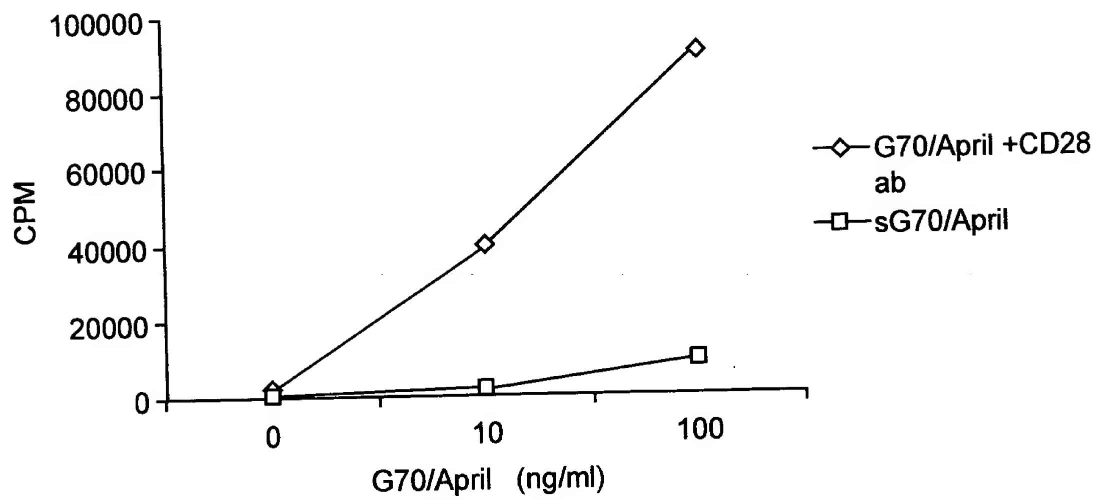


FIG. 9

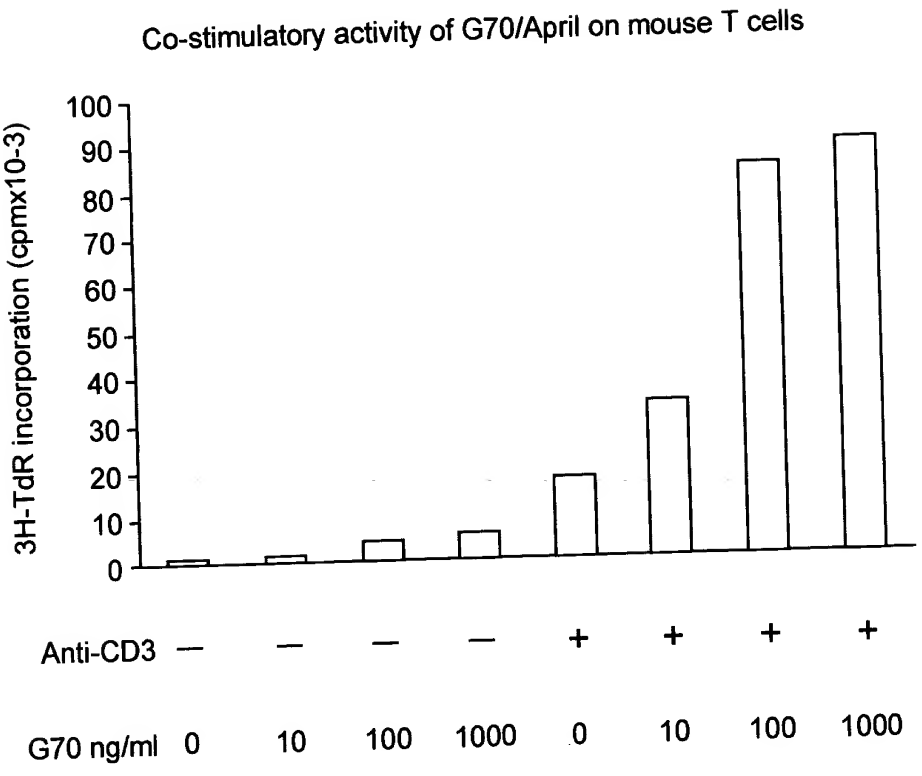

Co-stimulatory activity of G70/April on mouse T cells
3H-TdR incorporation (cpmx10-3)
100
90
80
70
60
50
40
30
20
10
0
Anti-CD3 — — — — + + + +
G70 ng/ml 0 10 100 1000 0 10 100 1000

FIG. 10A

Human BCMA

Human (SEQ ID NO: 5):

1 MAGQCSQNEY FDSLLHACIP CQLRCSSNTP PLTCQRYCNA SVTNSVKGTN

51 AILWTCLGLS LIISLAVFVL MFLLRKISSE PLKDEFKNTG SGLLGMANID

101 LEKSRTGDEI ILPRGLEYTV EECTCEDCIK SKPKVDSDHC FPLPAMEEGA

151 TILVTTKTND YCKSLPAALS ATEIEKSISA R

Human (SEQ ID NO: 5):

MAGQ**CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C**NASVTNSVK

GTNA ILWTCL GLSLIISLAV FVLMFLLRKI SSEPLKDEFK NTGSGLLGMA

NIDLEKSRTG DEIILPRGLE YTVEECTCED CIKSKPKVDS DHCFPLPAME

EGATILVTTK TNDYCKSLPA ALSATEIEKS ISAR

hBCMA's extracellular domain (SEQ ID NO: 6):

MAGQCSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY CNASVTNSVK

GTNA

hBCMA's cysteine-rich consensus region (SEQ ID NO: 7):

CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C

hBCMA's transmembrane region (SEQ ID NO: 8):

ILWTCL GLSLIISLAV FVLMF

FIG. 10B

huBCMA-Fc (SEQ ID NO: 9):

MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAGGG
GGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLSPGK*

muBCMA-Fc (SEQ ID NO: 10):

MAQQCFHSEYFDSLLHACKPCHLRCSNPPATCQPYCDPSVTSSVKGSYTGGGGG
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK*

FIG. 11

Alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence

murine BCMA amino acid sequence Length: 185 (SEQ ID NO: 11):

```
  1  MAQQCFHSEY FDSLLHACKP CHLRCSNPPA TCQPYCDPSV TSSVKGTYTV

 51  LWIFLGLTLV LSLALFTISF LLRKMNPEAL KDEPQSPGQL DGSAQLDKAD

101  TELTRIRAGD DRIFPRSLEY TVEECTCEDC VKSKPKGDSD HFFPLPAMEE

151  GATILVTTKT GDYGKSSVPT ALQSVMGMEK PTHTR
```

alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence.

```
Query:    4 MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAILWTCLGLS 63
            MA QC  +EYFDSLLHAC PC LRCS+  PP TCQ YC+ SVT+SVKGT  +LW  LGL+
Sbjct:    1 MAQQCFHSEYFDSLLHACKPCHLRCSN--PPATCQPYCDPSVTSSVKGTYTVLWIFLGLT 58

Query:   64 LIISLAVFVLMFLLRKISSEPLKDEFKNTG----SGLLGMANIDLEKSRTGDEIILPRGL 119
            L++SLA+F + FLLRK++ E LKDE ++ G     S  L  A+ +L + R GD+ I PR L
Sbjct:   59 LVLSLALFTISFLLRKMNPEALKDEPQSPGQLDGSAQLDKADTELTRIRAGDDRIFPRSL 118

Query:  120 EYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKS-LPAAL-SATEI 177
            EYTVEECTCEDC+KSKPK DSDH FPLPAMEEGATILVTTKT DY KS +P AL S   +
Sbjct:  119 EYTVEECTCEDCVKSKPKGDSDHFFPLPAMEEGATILVTTKTGDYGKSSVPTALQSVMGM 178

Query:  178 EKSISAR 184
            EK    R
Sbjct:  179 EKPTHTR 185
```

FIG. 12A

Human TACI

huTACI (SEQ ID NO: 14).

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYSTLGLC LCAVLCCFLV AVACFLKKRG DPCSCQPRSR

201 PRQSPAKSSQ DHAMEAGSPV STSPEPVETC SFCFPECRAP TQESAVTPGT

251 PDPTCAGRWG CHTRTTVLQP CPHIPDSGLG IVCVPAQEGG PGA

MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRS**CPEEQYWDPLLGTCMSC**
KTICNHQSQRTCAAFCRSLS**CRKEQGKFYDHLLRDCISCASICGQHPKQC**
AYFCENKLRSPVNLPPELRRQRSGEVENNSDNSGRYQGLEHRGSEASPAL
PGLKLSADQVALVYSTLGLCLCAVLCCFLVAVACFLKKRGDPCSCQPRSR
PRQSPAKSSQDHAMEAGSPVSTSPEPVETCSFCFPECRAPTQESAVTPGT
PDPTCAGRWGCHTRTTVLQPCPHIPDSGLGIVCVPAQEGGPGA

huTACI's extracellular domain (SEQ ID NO: 15):

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYST

FIG. 12B

huTACI's cysteine-rich consensus region (SEQ ID NO: 16):

CPEEQYWDPLLGTCMSCKTICNHQSQRTCAAFC and

CRKEQGKFYDHLLRDCISCASICGQHPKQCAYFC

transmembrane region (SEQ ID NO: 17):

LGLCLCAVLCCFLVAVACFL

hTACI-Fc (SEQ ID NO: 18):

```
  1  MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

 51  KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101  AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151  PGLKLSADQV ALVYSGGGGG DKTHTCPPCP APELLGGPSV FLFPPKPKDT

201  LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY

251  RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT

301  LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS

351  DGSFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK*
```

FIG. 13

Alignment of cysteine rich extracellular regions of human TACI and human BCMA.

```
34 CPEEQYWDPLLGTCMSCKTICNHQS.QRTCAAFCRSLSCRKEQGKFYDHL 82
   | : :|.| ||  |. |.  |.  .   ||  :| .      .|   . :
 8 CSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGT..NAI 55

      83 LRDCISCASI 92
         |  |:  . |
      56 LWTCLGLSLI 65
```

FIG. 14A

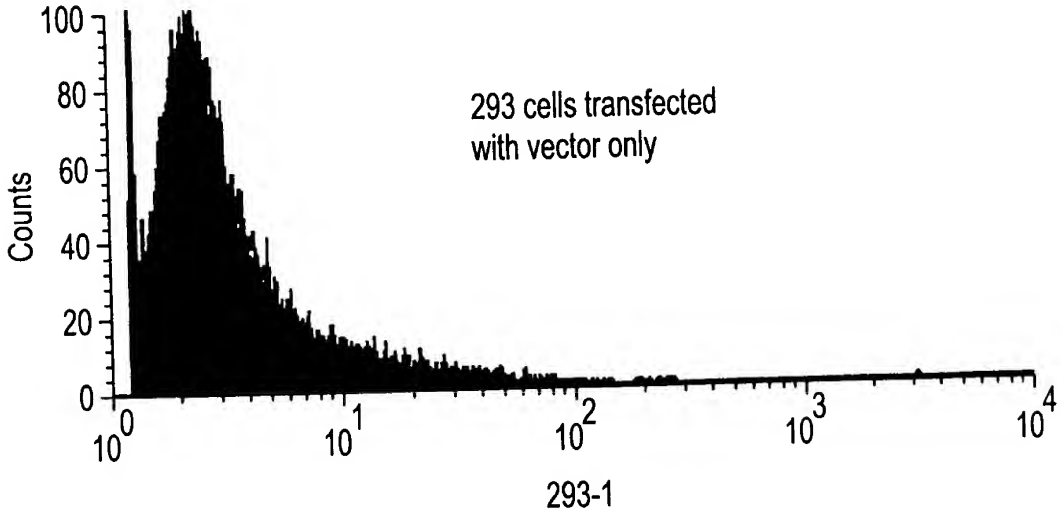


FIG. 14B

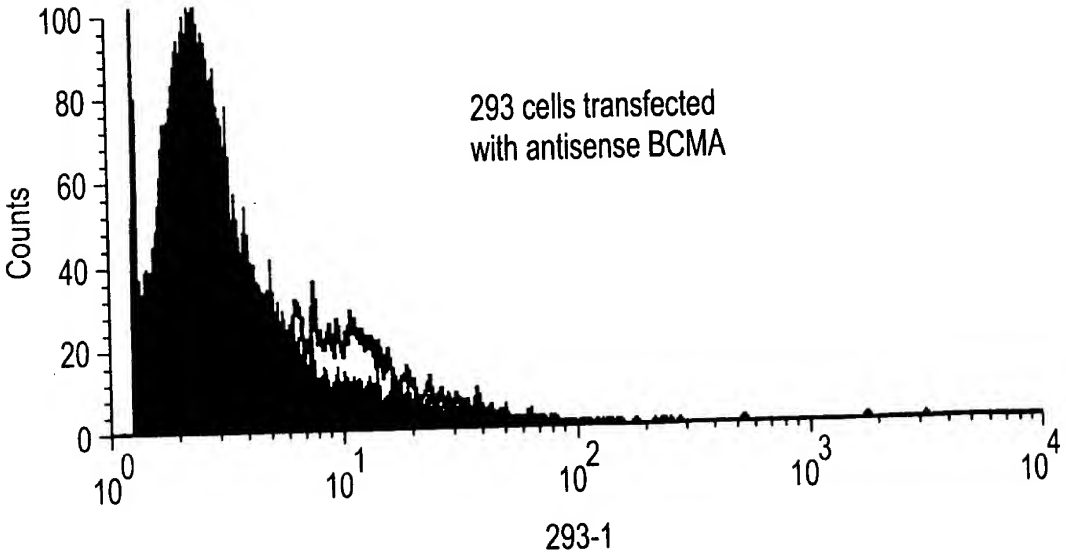


FIG. 14C

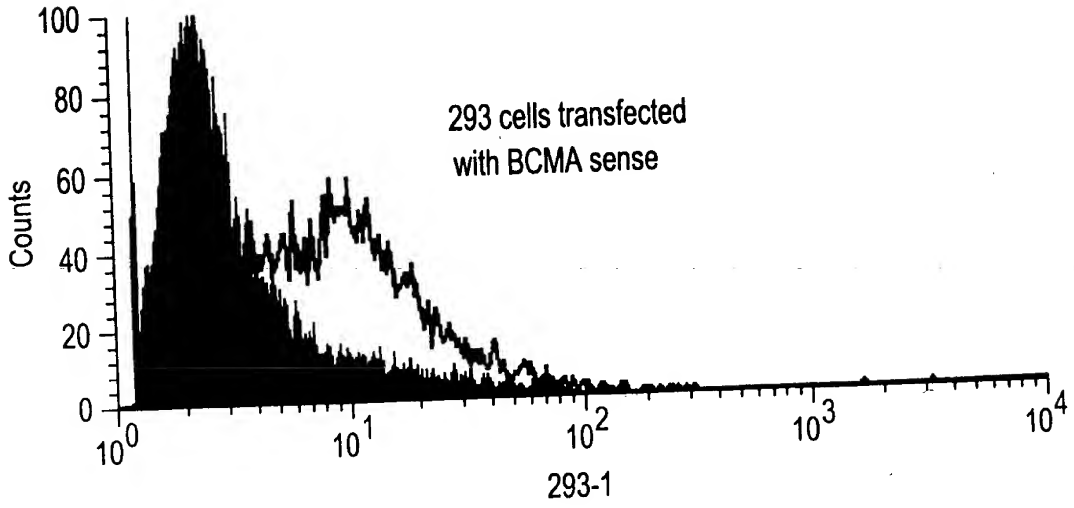

100
80
60
40
20
0
Counts
293 cells transfected
with BCMA sense
10^0
10^1
10^2
10^3
10^4
293-1

FIG. 15A

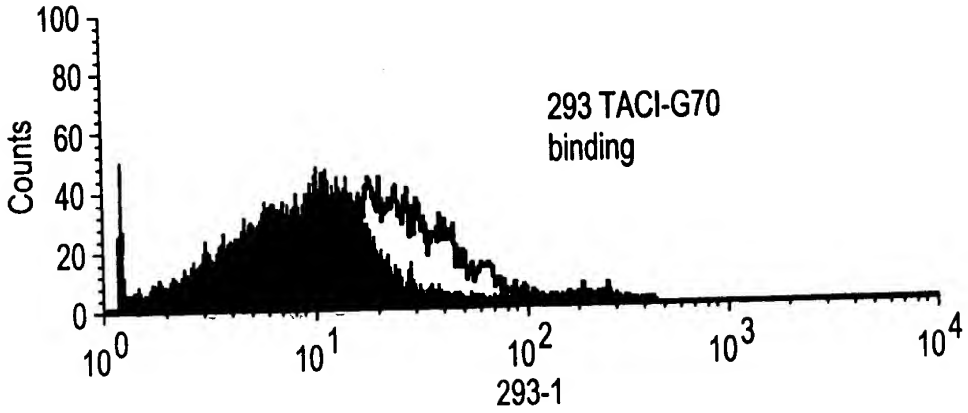


FIG. 15B

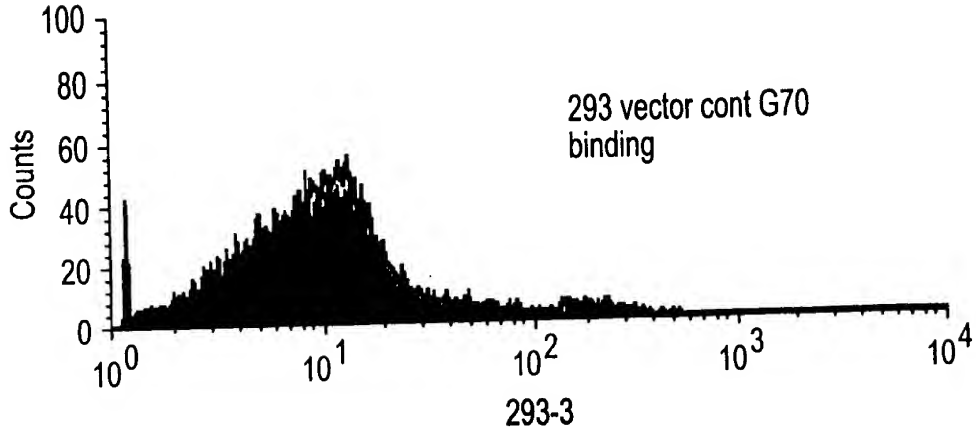


FIG. 16A

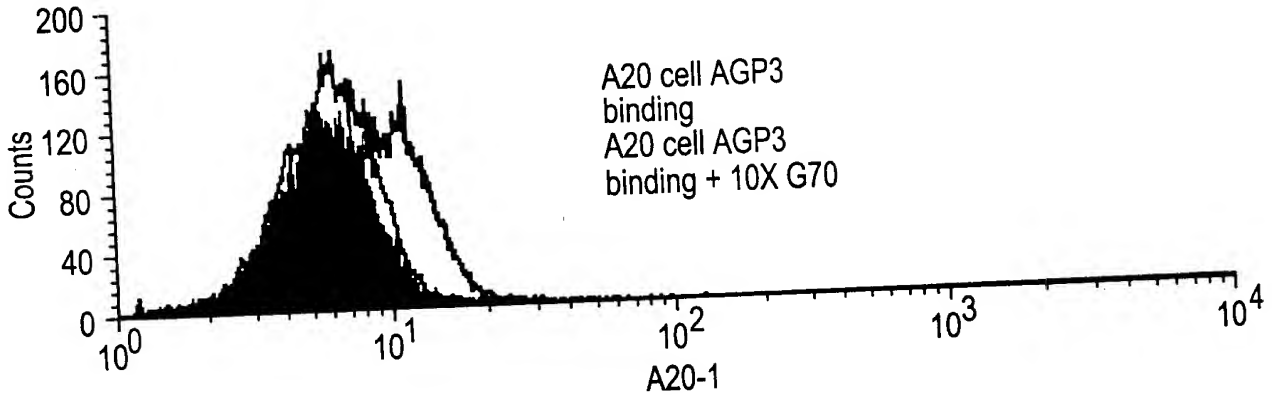
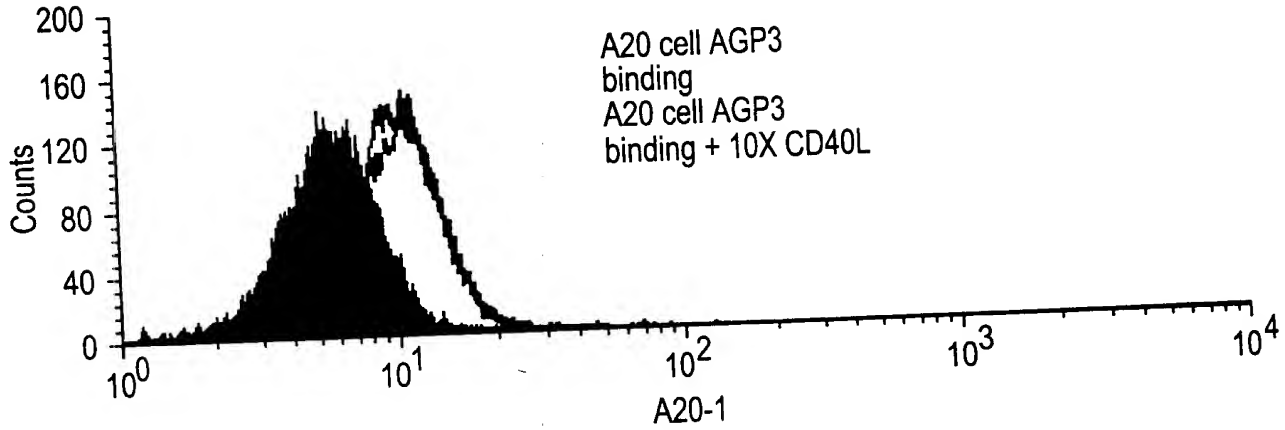


FIG. 16B



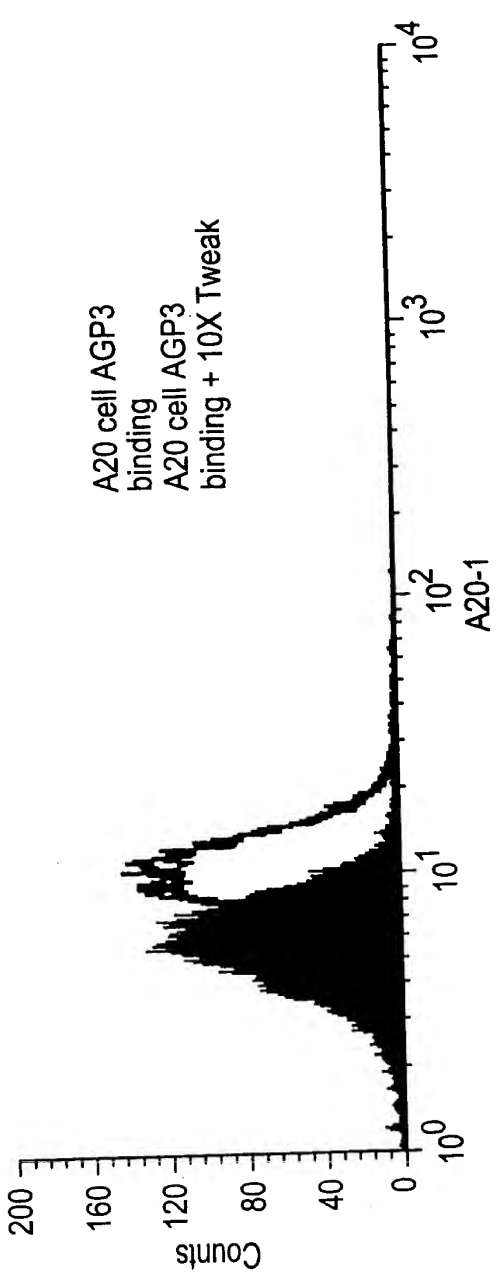


FIG. 16C

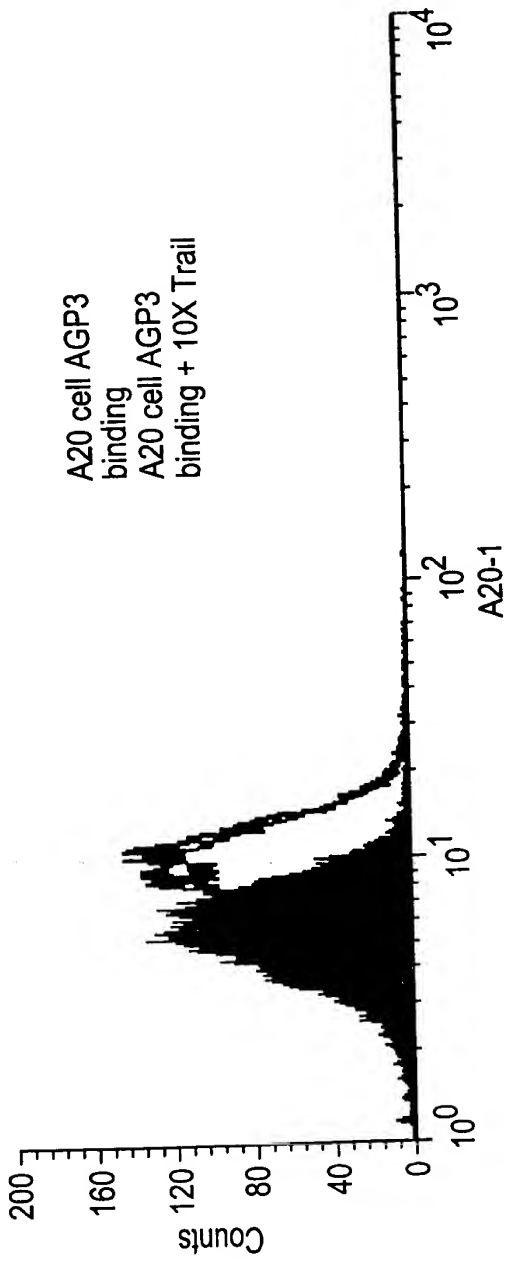


FIG. 16D

FIG. 17A

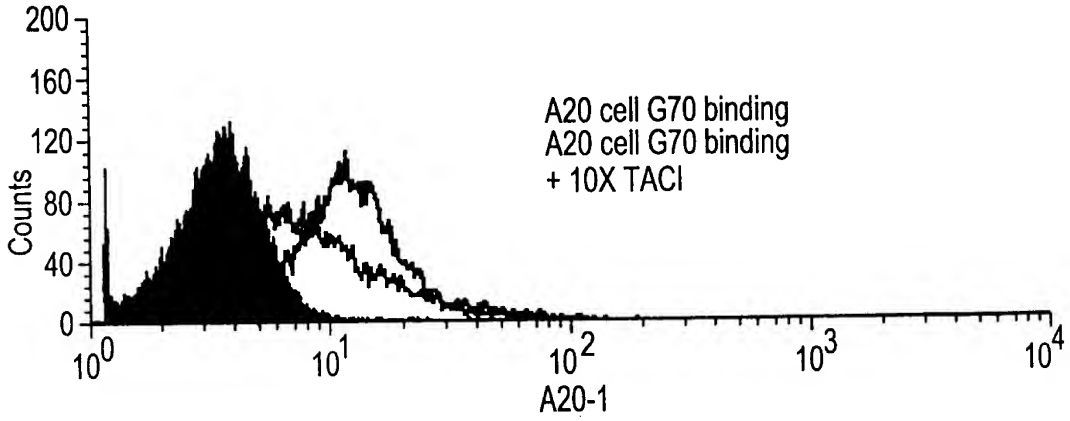


FIG. 17B

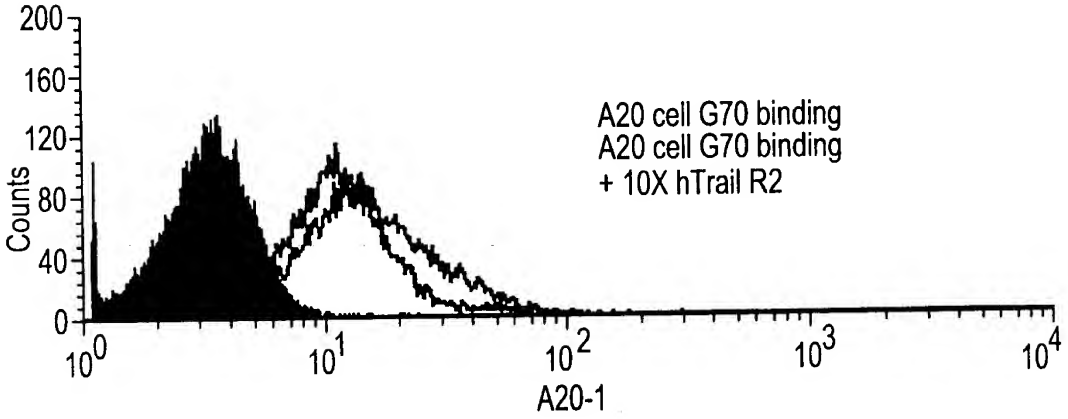


FIG. 17C

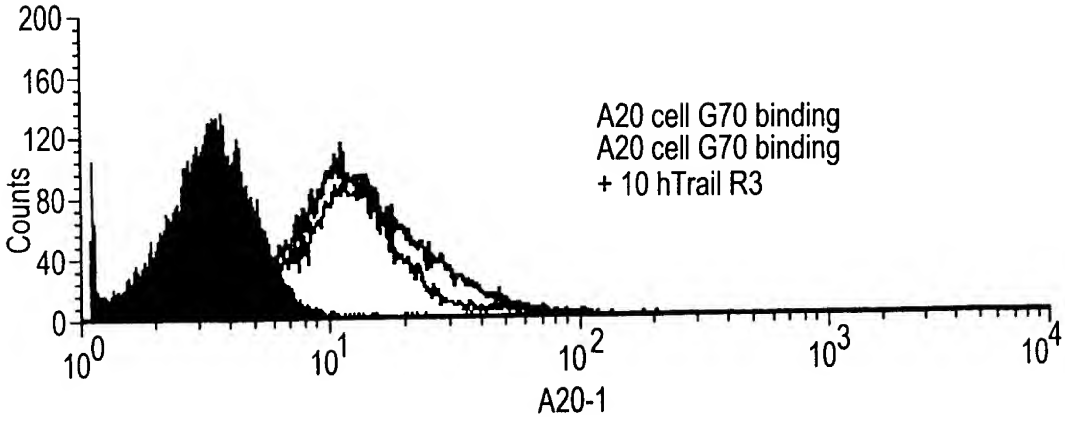


FIG. 18

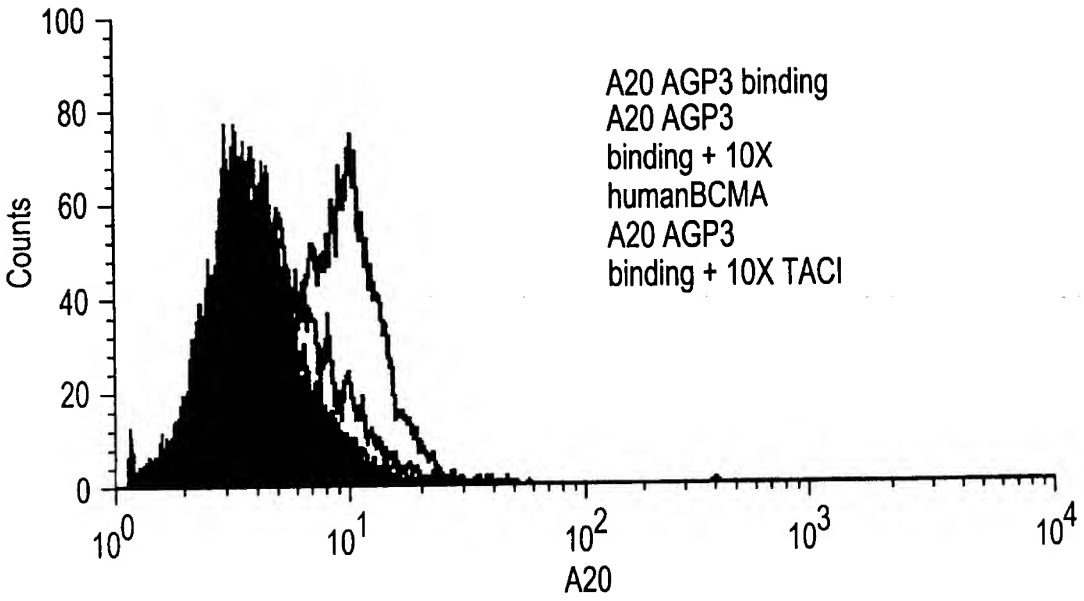

100
80
60
40
20
0
Counts
10^0
10^1
10^2
10^3
10^4
A20
A20 AGP3 binding
A20 AGP3 binding + 10X humanBCMA
A20 AGP3 binding + 10X TACI

FIG. 19A

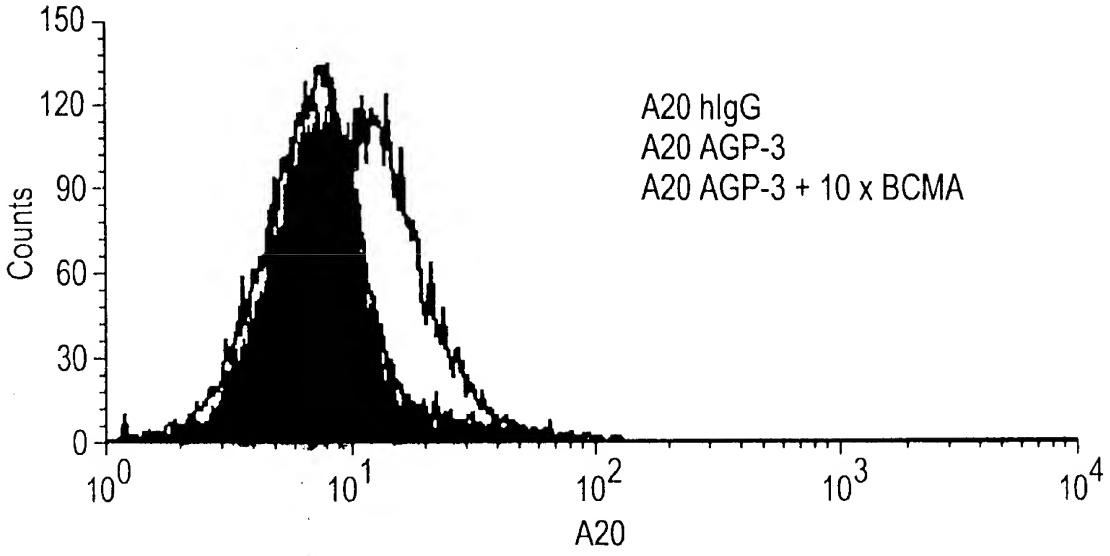


FIG. 19B

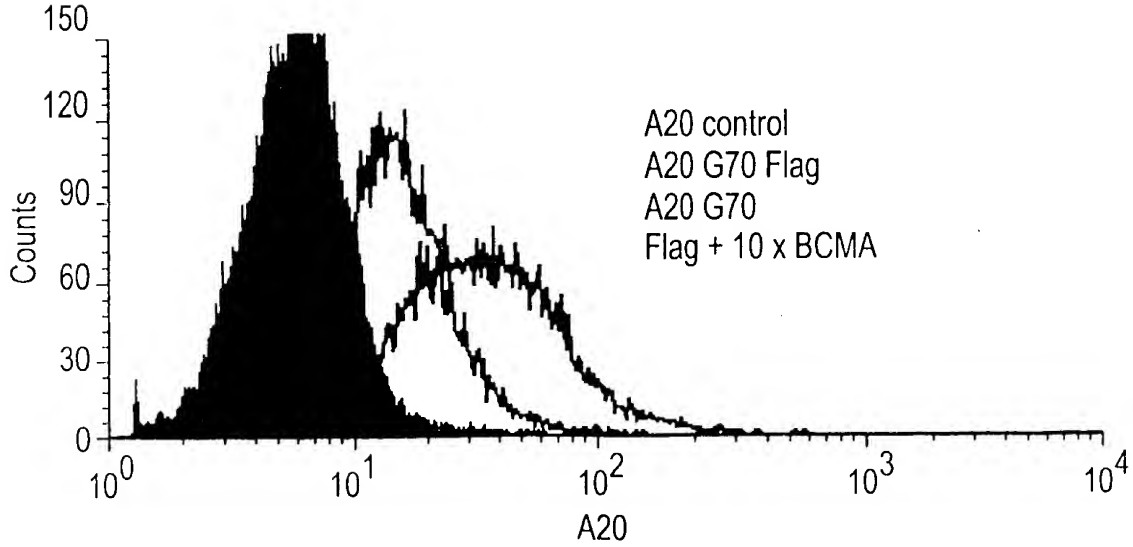


FIG. 20A

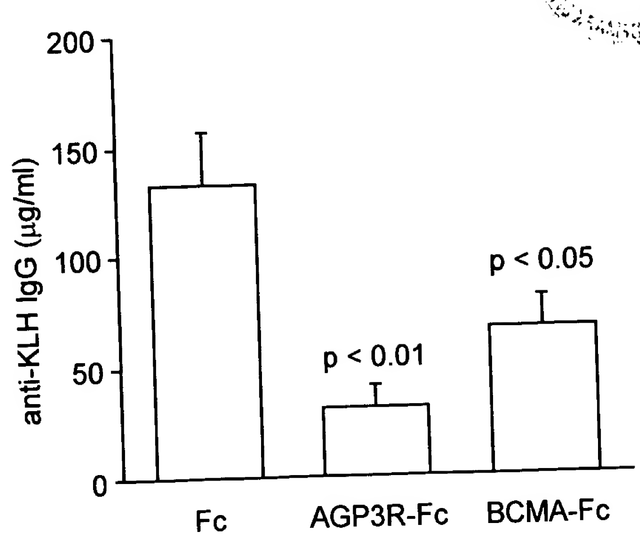


FIG. 20B

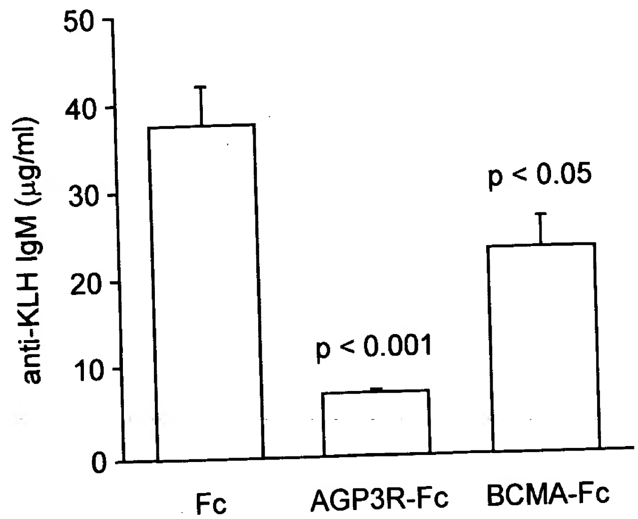


FIG. 20C